

AMENDMENTS TO THE SPECIFICATION

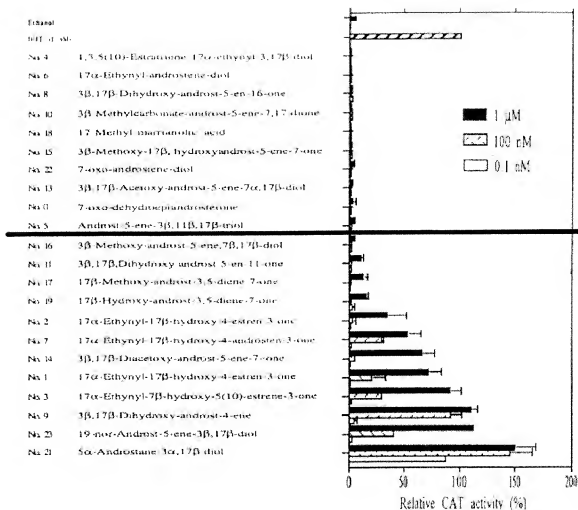
Please amend the specification as follows.

After the 'Detailed Description of the Invention' header on page 6, add the following new paragraph.

- 5 Brief description of the drawings. Figure 1: Effects of various DHEA metabolites on the transcriptional activity of AR. Figure 2A: The structures of compounds nos. 4, 6, 8, and 10, DHEA, Adiol, and testosterone. Figure 2B: CAT activity in PC-3 cells. Figure 3: The suppression effects of nos. 4, 6, 8, and 10 DHEA derivatives on the DHT-induced AR transcriptional activity. Figure 4: The
10 effects of nos. 4, 6, 8, and 10 DHEA derivatives on the Adiol-induced and HF-blocked AR transcriptional activity. Figure 5: The effects of nos. 4, 6, 8, and 10 DHEA derivatives on the ER, PR, or GR transcriptional activity.

Amend the paragraph beginning at page 79, line 9 as follows.

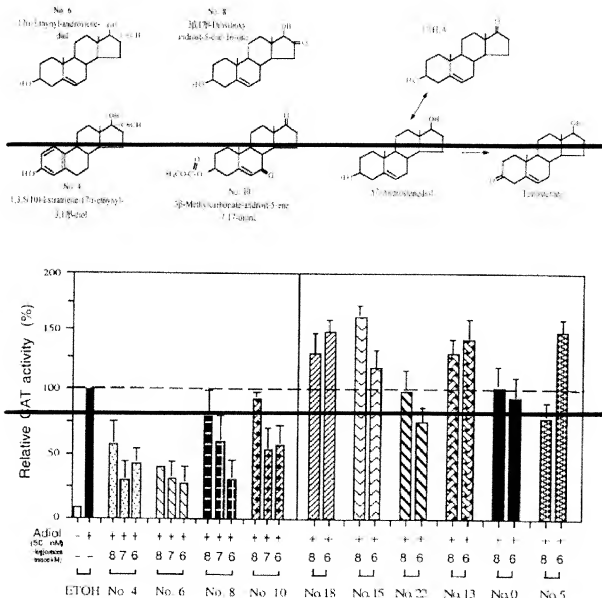
- 15 **Example 2. Induction of AR-mediated transcriptional activity.**



Steroid compounds were screened for their ability to induce AR transcriptional activity in the AR-negative PC-3 cell line. The results of the CAT assay were obtained by transient co-transfection of AR plasmid and a reporter plasmid (MMTVCAT) containing the CAT gene linked to the androgen response element (ARE). After transfection, the cells were treated with various DHEA derivatives at 1000, 10, and 0.1 nM. As shown in figure 1 above, compounds 0, 4, 5, 6, 8, 10, 13, 15, 16, 18, and 22 had little androgenic activity but they did induce a low level of AR-mediated CAT gene transactivation. AED (compound 21) had about the same capacity as DHT to stimulate AR-mediated CAT gene transcription.

Amend the paragraph beginning at page 80, line 6 as follows.

Example 3. Identification of anti-adiol activity of steroids with low androgenic effects.



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Several compounds were screened for their capacity to modulate AED's effects on AR-mediated activation of gene transcription in PC-3 cells. The chemical structures of compounds 4, 6, 8 and 10 are shown in figure 2A above. The PC-3 cells were co-transfected with pSG5 and the MMTV-CAT reporter vector in the presence of 50 nM AED and each compound at a concentration of 10, 100, or

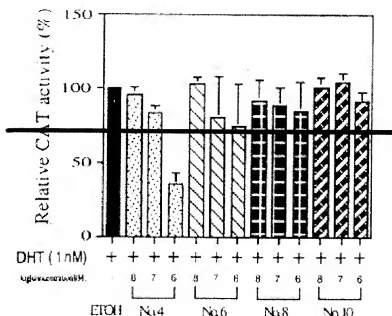
10

1000 nM. As shown in figure 2B above, compounds 4, 6, 8 and 10 antagonized AED-mediated AR transcriptional activity. At concentrations of 0.1 μ M and 1 μ M, compounds 4 and 6 suppressed the AED-induced AR transactivation to less than 30%. Compounds 0, 5, 13, 15, 18 and 22 show either activation of

5 AED-mediated AR transcriptional activity or they have no effect.

Amend the paragraph beginning at page 80, line 17 as follows.

Example 4. Identification of anti-DHT effects of steroids.

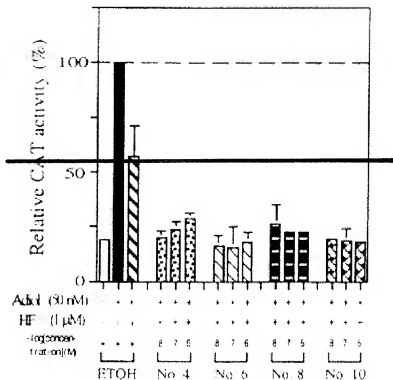


10 Compounds 4, 6, 8 and 10 were examined to determine whether these AED antagonists had the ability to repress DHT-induced AR transactivation. PC-3 cells were co-transfected with pSG5 and the MMTV-CAT reporter plasmid in the presence of 1 nM DHT and each compound at 10, 100, or 1000 nM. Compound

15 4 repressed the DHT-induced AR transactivation to less than 40% at 1 μ M (figure 3) as shown above.

Amend the paragraph beginning at page 80, line 23 as follows.

Example 5. Suppression of the AED-induced AR transcriptional activity in the presence of HF.



To mimic the *in vivo* condition of total androgen blockage in prostate cancer

- 5 patients, compounds 4, 6, 8 and 10 were examined for their capacity to antagonize AED-induced AR transactivation in the presence of HF. In the presence of 1 μ M HF, 50 nM AED, and each compound at 0.01, 0.1 or 1 μ M, PC-3 cells were transiently transfected with pSG5 and the MMTV-CAT reporter plasmid. As shown in figure 4 above, HF suppressed AED-mediated AR
- 10 transcription activity by about 40%. The compounds tested decreased AED-mediated AR transcription activity by about 75%.